



PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: George A. Doherty, et al.

Serial No.: 10/500,811 Case 21020P

Filed: July 7, 2004

For: N-BENZYL AMINOALKYLCARBOXYLATES,
PHOSPHINATES, PHOSPHONATES AND
TETRAZOLES AS EDG RECEPTOR AGONISTS

Art Unit:

1626

Examiner:

Anderson, Rebecca L.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO RESTRICTION REQUIREMENT

Sir:

This communication is in response to the restriction requirement dated February 12, 2007, setting forth a shortened statutory period for response ending March 12, 2007. Reconsideration of the restriction requirement and allowance of the above-captioned patent application are respectfully requested. This application relates to N-benzyl aminoalkylcarboxylates, phosphinates, phosphonates and tetrazoles as edg receptor agonists.

Claims 1 to 22, 34 and 35 are currently pending in the application. The Examiner has required restriction of Claims 1 to 22, 34 and 35 and an election of one of **Group I** to **Group XXIV** as outlined in the Restriction Requirement dated February 12, 2007. **Group V** is hereby elected with traverse. Applicants also hereby elect the specie of Example 144 (structure shown at page 34), with traverse. Inasmuch as the Examiner requires election of a single disease to be treated, Applicants elect transplantation of organs or tissue.

Applicants respectfully request reconsideration of the restriction requirement with respect to Claims 1 to 22, 34 and 35 and submit that these claims satisfy the unity of invention requirement because the groups are properly linked to form a single general inventive concept. As outlined in M.P.E.P. § 1893.03(d), a group of inventions is considered linked to form a single

general inventive concept when there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. The expression "special technical feature" is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art.

With respect to "Markush Practice," Annex B of the PCT Administrative Instructions sets forth the standard of unity of invention as follows:

(f) "Markush Practice." The situation involving the so-called "Markush practice" wherein a single claim defines alternatives (chemical or non-chemical) is also governed by Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

(i) When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

- (A) all alternatives have a common property or activity, and*
- (B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or*
- (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.*

(ii) In paragraph (f)(i)(B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

In the instant claims, the special technical feature is the novel and non-obvious core structure embodied in Formula I. All compounds share this significant common chemical structure which occupies a large portion of their structures. The claimed compounds also possess the same utility as edg receptor agonists and for treating diseases or conditions mediated by that receptor. As such, unity of invention is present.

On page 5 of the Restriction Requirement, the Examiner alleges that the technical feature corresponding to the claims is C-N-C and that this technical feature is not a special technical feature because it fails to make a contribution over the prior art. Applicants respectfully submit the Examiner's analysis is incorrect. The PCT Administrative Instructions clearly state that special technical features as defined in Rule 13.2 shall be considered to be met when the alternatives are of a similar nature. A Markush grouping of chemical compounds shall be regarded as being of similar nature when all alternatives have a common property and there is a significant structural element shared by all the alternatives. The term "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art. Thus, an analysis as to whether the commonly shared structure constitutes a structurally distinctive portion in view of the prior art would only be required in the latter case. Since the instant claims are directed to compounds that share a common chemical structure that occupies a large portion of their structures, an analysis under the second part is not required.

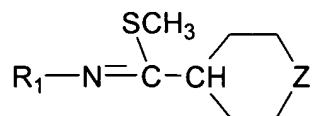
Furthermore, Applicants submit the Examiner has improperly applied the unity of invention standard with respect to Markush practice in defining the technical feature as C-N-C. As stated previously, a technical feature is deemed a special technical feature for purposes of Markush practice when the alternatives are of a similar nature, i.e., when all alternatives have a common property and there is a significant structural element shared by all the alternatives. The Examiner's narrow definition of C-N-C alone does not constitute the significant structural element shared by all the alternatives as defined in Annex B of the PCT Administrative Instructions. The Examiner seems to be taking the position that because groups such as Ar, which can be phenyl or naphthyl, or A, which is an acidic group, can vary that they cannot form

part of the common chemical structure. This is the incorrect standard for unity of invention with respect to Markush practice.

In support of this argument, Applicants refer the Examiner to Chapter 10 of the PCT International Search and Preliminary Examination Guidelines. These guideline set forth examples concerning unity of invention. § 10.39 reads as follows:

Example 19: common structure:

Claim 1: A compound of the formula:



wherein R₁ is selected from the group consisting of phenyl, pyridyl, thiazolyl, triazinyl, alkylthio, alkoxy, and methyl; Z is selected from the group consisting of oxygen (O), sulfur (S), imino (NH), and methylene (-CH₂-).

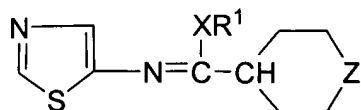
The compounds are alleged to be useful as pharmaceuticals for relieving lower back pain.

In this particular case the iminothioether group -N=C-SCH₃ linked to a six atom ring is the significant structural element which is shared by all the alternatives. Thus, since all the claimed compounds are alleged to possess the same use, unity would be present.

§ 10.40 reads as follows:

Example 20: Common Structure

Claim 1: A compound of the formula:



wherein R^1 is methyl or phenyl, X and Z are selected from oxygen (O) and sulfur (S).

The compounds are useful as pharmaceuticals and contain the 1,3-thiazolyl substituent which provides greater penetrability of mammalian tissue which makes the compounds useful as relievers for headaches and as topical anti-inflammatory agents.

All compounds share a common chemical structure, the thiazole ring and the six atom heterocyclic compound bound to an imino group, which occupy a large portion of their structure. Thus, since all the claimed compounds are alleged to possess the same use, unity would be present.

Under the Example 19 above, the "significant structural element" contains a "six atom ring." The Examiner should note that this six-membered ring can vary with respect to three different heteroatoms, i.e., oxygen, sulfur and imino, and a non-heteroatom, methylene. Under Example 20, the "significant structural element" contains a "six atom heterocyclic compound," which can vary as containing oxygen and sulfur. Clearly, if such divergent groups contained in a "six-membered ring" are allowable under unity of invention practice, then Ar equal to phenyl or naphthyl in the present claims should also be considered as part of the significant structural element, particularly considering the relation between the structures and properties of phenyl and naphthyl.

Likewise, the substituent A corresponds to acidic groups and as such should also be considered part of the "significant structural element." The common structure also requires the substitution -B-C, which is significant in length.

In the instant case, the Examiner has failed to include all the structural elements in her definition of C-N-C as the technical feature and has not utilized the appropriate unity of invention standard for Markush practice. In the instant claims, the compounds share a common chemical structure that occupies a large portion of their structures and which therefore constitutes a significant structural element shared by all the alternatives. All alternatives have a common activity as edge receptor agonists. Thus, the claimed alternatives of chemical

compounds are regarded as being of a similar nature and thus constitute a special technical feature as defined in PCT Rule 13.2. Unity of invention is therefore present.

Applicants also disagree with the Examiner's assertion that the "variables ... vary extensively and when taken as a whole result in vastly different compounds." Applicants submit this is not the proper standard for unity of invention. As stated in the PCT Administrative Instructions, Annex B, (f)(iv): the "fact that the alternatives of a Markush grouping can be differently classified shall not, taken alone, be considered to be a justification for a finding of a lack of unity of invention."

Applicants also respectfully disagree with the Examiner's statement that the "vastness of the claimed subject matter, and the complications in understanding the claimed subject matter impose a serious burden on any examination of the claimed subject matter." Applicants not only submit that this is also not a consideration in a unity of invention determination, but that the claims are in no way too vast or overly complicated.

At page 5 of the Official Action, the Examiner states the following:

... even if unity of invention under 37 CFR 1.475(a) is not lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to only one of the following combinations: And, according to 37 CFR 1.475, if an application contains more or less that one of the combinations of categories of invention set forth in paragraph (b), unity might not be present.

Applicants submit that the Examiner's reading of 37 C.F.R. § 1.475 is improper. 37 C.F.R. §§ 1.475 (b) and § 1.475 (c) do not constitute a separate standard of unity of invention independent of 37 C.F.R. § 1.475(a). As stated in M.P.E.P. § 1893.03(d): "37 CFR 1.475 was amended effective May 1, 1993 to correspond to PCT Rule 13." Furthermore, 37 C.F.R. § 1.475(c) states only that "unity of invention might not be present. (emphasis added)" In the instant case, there is a special technical feature common to Claims 1 to 22, 34 and 35 as described above. Unity of invention exists with respect to Claims 1 to 22, 34 and 35 under PCT Rule 13 and 37 C.F.R. § 1.475.

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Even if the Examiner disagrees with the Applicants that the product and method claims should not be restricted, Applicants submit that the Examiner is required to rejoin any withdrawn method of treatment claims which depend from allowable compound/pharmaceutical composition claims pursuant to M.P.E.P. § 821.04.

Applicants respectfully request reconsideration and withdrawal of the requirement for restriction. Applicants submit that the application is in condition for allowance and passage thereto is earnestly requested. Any additional fees required in connection with this Response may be taken from Merck Deposit Account No. 13-2755. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of the case.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

By [Signature] Date 12-MAR-2007

Date: March 12, 2007

Respectfully submitted,

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